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EXAMINER	
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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,037	POULIQUEN ET AL.	
	Examiner	Art Unit	
	ILEANA POPA	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *24-27 and 30-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,28 and 29* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/21/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of the invention of Group I (drawn to a composition comprising a polymer and an interferon) and of species of polyglutamate and IFNα in the reply filed on 11/02/2009 is acknowledged. The traversal is on the ground(s) that the reasons given by the Office for the species allegedly lacking the same or corresponding special technical features are improper. Applicant argues that Rule 13.2 of the Regulations Under the Patent Cooperation Treaty ("PCT Rules") states:

> Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions~ considered as a whole~ makes over the prior art.

(Rule 13.2. See also MPEP § 1850, page 1800-96). Applicant also directs the Examiner's attention to page 1800-99 of the MPEP, which states:

> Unity of invention has to be considered in the first place only in relation to the independent claims in an international application and not the dependent claims. If the independent claims avoid the prior art and satisfy the requirement of unity of invention, no problem of lack of unity arises in respect of any claims that depend on the independent claims. In particular, it does not matter if a dependent claim itself contains a further invention.
>
> (MPEP § 1850, page 1800-99).

Applicant submits that the independent claims of the application are patentable over the prior art.

A finding of anticipation by a reference requires that the reference teach all limitations of the anticipated claims. USPN 6,630,171 (corresponds to FR 2 786 098). USPN 6,630,171 fails to meet this requirement at least because it fails to teach formulations that include a surfactant, which is a feature that is shared by all claims. Accordingly, all of the claims do share a special technical feature and thus do possess unity of invention.

Applicant's arguments are acknowledged; however, they are not found persuasive because the presence of a surfactant in claim 1 is optional. Therefore, the independent claim 1 is anticipated by USPN 6,630,171 and does not satisfy the requirement of unity of invention. The requirement is still deemed proper and is therefore made FINAL.

However, because a search for the elected species of polyglutamate rendered results relevant for the species of polyaspartate and aspartate/glutamate co-polymers, the claims directed to these species are hereby rejoined.

Claims 24-27 and 30-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim.

Claims 4-6, 9, 11, 17-23 and 28 have been amended.

Claims 1-23, 28 and 29 are under examination.

Priority

2. It is acknowledged that a certified foreign priority paper has been received. It is noted however that an English translation has not been provided.

Claim Objections

3. Claim17 is objected to because of the following informalities: the claim recites "1% ≤ [n/(n+m)] x ≤ 100 10%". Appropriate correction to "1% ≤ [n/(n+m)] x 100 ≤ 10%" is required.

Claim Rejections - 35 USC § 112, 2nd paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 2, 4-12, 16-23 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

At issues are the following recitations:

- Claim 4: "≥ 0.9.C1, preferably 20.C1 ≥ [PO] ≥ C1, and particularly preferably 10.C1 ≥ [PO] ≥ C1";

- Claims 7 and 8: "cations based on polyamine (polyethylenimine being particularly preferred)", "n/(n+m) varies between 0.5 and 100 mol%, preferably being between 1 and 25 mol% and particularly preferably between 1 and 15 mol%" and "n+m varies from 10 to 1000 and preferably between 50 and 300";

- Claim 10: "at least one heteroatom (preferably O and /or N and/or S);

- Claim 16 "between 2000 and 100,000 g/mol, preferably between 5000 and 40,000 g/mol";

- Claims 17 and 18: "1% ≤ [n/(n+m)] x 100 ≤ 10%, preferably 3.5% ≤ [n/(n+m)] x 100 ≤ 7.5%, n+m varies from 100 to 400 and preferably between 120 and 300;

- Claim 21: "polysaccharides (preferably those in the subgroup comprising pullulans and/or chitosans and/or mucopolysaccharides)";

- Claim 22: "non-associated interferon ≤ 1, preferably non-associated interferon ≤ 0.5.

A preferred embodiment may be set forth in another dependent claim; when stated in a single claim, preferences lead to confusion over the intended scope of the claim. Since it is not clear whether the claimed preferred embodiment (i.e., completely water-soluble) is a claim limitation, the metes and bounds of the claims cannot be determined and the claim is indefinite.

Claims 1, 2, 5, 6, 9, 11, 12, 19-21, 23 and 28 are included in the instant rejection because claims 4, 7, 8, 10, 16-18 and 22 directly or indirectly depend from claim 1. Therefore, claim 1 and its remaining dependent claims encompass the embodiments under rejection.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees.

A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-23, 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-10, 12-22, 25, 26, 28, 29, 35 and 36 of copending Application No. 10/580,035. Although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to the same polymer formulation for prolonged delivery of therapeutic agents. Although the instant claims recite interferon and not interleukin, one of skill in the art would have found it obvious to replace the interleukin with interferon.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 1-23, 28 and 29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20, 25 and 27

of copending Application No. 11/878,947, over claims 1-16, 21, 22, 24-26, 28 and 29 of copending Application No. 10/580,023, over claims 1-16, 21, 22, 24-26, 28 and 29 of copending Application No. 10/580,023, over claims 1-19, 22, 25, 28, 29, 34 and 35 of the copending Application No. 11,808,456, over claims 1-10, 15, 17-24 and 26 of the copending Application No. 10/516,733, over claims 1-3, 5-11, 13-16 and 18-22 of the copending Application No. 11/658,803 and over claims 1-4, 6-11, 15, 16, 18-21, 26-30, 38 and 39 of the copending Application No. 12/003,095. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the applications claims are drawn to the same polymer formulation for prolonged delivery of therapeutic agents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 1-23, 28 and 29 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-21, 28-32 and 40 of U.S. Patent No. 6,630,171. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims and the patent claims are drawn to the same polymer formulation for prolonged delivery of interferon. Although the patent claims do not recite gel-forming properties, such properties are inherent to the patent composition.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 6, 7, 16, 18, 21 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Huille et al. (WO 00/30618 Applicant's IDS). The English language translation of WO 00/30618 is US Patent 6,630,171. The passages cited below which indicate the teachings of the '618 publication are based on its English translation (i.e., the '171 patent).

Huille et al. teach a liquid, low viscosity formulation suitable for parenteral injection and prolonged release of interferon, wherein the formulation is liquid in physiological medium and wherein the formulation comprises an aqueous colloidal suspension of submicronic particles in water and interferon(IFN) non-covalently-associated with the particles. The particles are made of homopolymers of α-aspartate or α-glutamate or of aspartate/glutamate copolymers (i.e., water-soluble polymers) carrying hydrophobic groups (HG), the HG could be cholesterol, the molar grafting rate is between 3 and 70%, the polymers contain up to 200 amino acids (i.e., n+m is 200) and the molecular weight of the polymer could be 20,000 g/mol; the polymers could have a structure as set forth in formula I (claims 1, 6, 7, 16, 18, 21 and 28) (Abstract, column 3, lines 25-65, column 4, lines 6-65, column 5, lines 45-61, column 9, lines 35-41, Example 1). With respect to the limitations of the formulation being able to form a gel *in vivo* in the presence of one physiological protein, wherein forming a gel makes it

possible to control the *in vivo* release of IFN (claim 1), such are functional descriptions of the structures recited in the claims and are inherent to the structure of the composition. The formulation of Huille et al. is identical to the instant formulation; therefore the formulation of Huille et al. must necessarily be capable of forming a gel *in vivo* for IFN release beyond 24 h. Since Huille et al. teach all the claim limitations, the claimed invention is anticipated by the above-cited art.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1, 5-8, 12-16, 18, 20-23 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al., in view of Edwards et al. (Arch. Dermatol., 1990, 126: 1029-1032, Abstract).

The teachings of Huille et al. are applied as above for claims 1, 6, 7, 16, 18, 21, and 28. Although Huille et al. do not specifically teach their low viscosity formulation as having a viscosity of up to 5Pas at 20°C (claims 5 and 20), it would have been obvious to one of skill in the art, at the time the invention was made, to vary the viscosity of their formulation with the purpose of optimizing the results.

Huille et al. do not specifically teach a polymer having formula IV (claim 8). However, it is noted that there is no evidence on the record that the claimed HG

arrangement result in a polymer exhibiting an unexpected property. The arrangement is not significant if it does not provide a novel feature. Moreover, it would have been obvious to one of skill in the art to vary the arrangement, with the purpose to achieve the optimum results. Absent evidence to the contrary, it is generally not inventive to discover the optimal arrangement of a prior art composition, such can be identified by routine experimentation.

Although Huille et al. teach homopolymers of α-aspartate or α-glutamate, they do not specifically teach that the amino acid precursors are L-aspartate or L-glutamate (claim 12-14). However, it would have been obvious to one of skill in the art to use such to achieve the predictable result of obtaining a polymer suitable for the controlled release of IFN. With respect to claim 15, Huille et al. teach their polymers as being either random or block polymers (column 7, lines 58-60).

Although Huille et al. teach a degree of association for insulin > 90% (Example 7), they do not specifically teach the same degree for IFN (claim 22). However, one of skill in the art would have reasonably expected to obtain the same high degree of association when using IFN.

Although Huille et al. teach IFN, they do not specifically teach IFN-α (claim 23). Edwards et al. teach treatment of basal cell carcinoma via administration of controlled-release formulation comprising IFN-α (Abstract). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the formulation of Huille et al. by substituting their IFN with IFN-α to achieve the predictable result of obtaining a formulation suitable for the controlled-release of IFN-α.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

14. Claims 1-4, 6, 7, 16, 18, 21, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over of Huille et al., in view of each Eliaz et al. (J. Biomed. Mater. Res., 2000, 50: 388-396), Regalado et al. (Macromolecules, 1999, 32: 8580-8588, Applicant's IDS) and Akiyoshi et al. (Macromolecules, 1997. 30: 857-861).

The teachings of Huille et al. are applied as above for claims 1, 6, 7, 16, 18, 21, and 28. Huille et al. do not specifically teach a polymer concentration which allows the formation of a gel deposit *in vivo* in the presence of at least one physiological protein (claims 2 and 29). However, doing such is suggested by the prior art. For example, controlled and prolonged drug release via using injectable formulations capable of gelling *in vivo* was routine in the prior art (see Eliaz et al., Abstract, p. 388, column 2). The prior art also teaches that incorporation of HG (including cholesterol) into hydrophilic polymers results in amphiphilic polymers which are capable of sol to gel transition and of forming gels after administration *in vivo*; formation of gels *in vivo* contributes to the sustained release of encapsulated drugs (see Regalado et al., p. 8580, column 1; Akiyoshi et al. p. 857, column 1). Based on these teachings in the art as a whole, one of skill in the art would have reasonably expected that the polymer of Huille et al. would also be capable of sol to gel transition and would have been motivated to vary the polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel *in vivo*. It is

noted that by doing such, one of skill in the art would have obtained a formulation capable of forming a gel deposit in the presence of physiological proteins, wherein the formulation comprises a concentration of polymer as recited in claim 4. With respect to claim 3, Huille et al. teach suspending their particles in aqueous solutions comprising BSA (Example 7); by varying the polymer concentration, one of skill in the art would have obtained a formulation wherein the polymer concentration is suitable of forming a gel *in vitro* in the presence of a protein.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

15. Claims 1, 6, 7, 16-19, 21, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al., in view of both Kim et al. (U.S. Patent No. 5,869,703) and Seo et al. (U.S. Patent No. 7,311,901).

The teachings of Huille et al. are applied as above for claims 1, 6, 7, 16, 18, 21, and 28. Huille et al. do not teach tocopherol (claim 17). However, using tocopherol to obtain biocompatible amphiphilic polymers is taught by the prior art (see Kim et al., column 1, lines 9-18, column 2, lines 20-55; Seo et al., Abstract, column 4, lines 10-30). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the polymer of Huille et al. by substituting their cholesterol with tocopherol to achieve the predictable result of obtaining a polymer suitable for prolonged IFN delivery. With respect to claim 19, it would have been obvious to one of skill in the art to vary the

polymer concentration such as to determine the proper concentration needed to obtain a liquid formulation capable to form a gel *in vivo*.

Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

16. Claims 1, 6, 7, 9-11, 16, 18, 21, and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huille et al., in view of Conover et al. (Anti-Cancer drug Design, 1999, 14: 499-506).

The teachings of Huille et al. are applied as above for claims 1, 6, 7, 16, 18, 21, and 28. Huille et al. do not teach coupling their cholesterol via an amino acid spacer (claims 9-11). However amino acid spacers (including alanine and phenylalanine) were routinely used in the prior art to create polymers suitable for drug delivery (see Conover et al., Abstract, p. 502, Tables I and II, p. 504, column 1). It would have been obvious to one of skill in the art, at the time the invention was made, to modify the polymer of Huille et al. by using an amino acid spacer to couple the cholesterol to their polymer to achieve the predictable result of obtaining a polymer suitable for sustained release of TNF. Thus, the claimed invention was *prima facie* obvious at the time the invention was made.

17. No claim is allowed. No claim is free of prior art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILEANA POPA whose telephone number is (571)272-5546. The examiner can normally be reached on 9:00 am-5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ileana Popa/
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